IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Ernest J. Lee, et al.	**Examiner:**	Schlientz, Nathan
Serial No.:	10/626,275	**Art Unit:**	1616
Filed:	July 24, 2003	**Atty Docket:**	PC28017
Title:	PRAMIPEXOLE ONCE-DAILY DOSAGE FORM		

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request. A Notice of Appeal is intended to be filed accompanying this paper. In the event that it does not, such appeal is requested. A Request for Extension is also intended to accompany this paper. In the event that it does not, an appropriate extension is requested. The Commissioner is authorized to charge any required fee to Deposit Account No. 16-1445.

This review is requested for the following reasons.

The 35 U.S.C. §112 rejections

Applicants believe the final rejections of claims 1, 3-10, 12-15, 20, 24, 25 and 28-41 and separately of claim 15 under 35 U.S.C. §112, second paragraph, as being indefinite are based upon a clear legal and factual deficiency.

The first ground of rejection derives from the use of the term "about" in several instances in the claims.

Applicants have cited a number of representative decisions from the Board of Patent Appeals and Interferences and from the Court of Appeals for the Federal Circuit which clearly

hold that use of the term "about" does not necessitate an indefiniteness rejection (see, e.g., pages 10-12, of applicants' Response filed December 16, 2010). These legal precedents clearly support the position that the fact that the term results in the absence of a mathematical certainty or precision as to the value does not mean the term is indefinite. Even absent such precision, the term does not give rise to indefiniteness if it would be understood by those of ordinary skill in the art. See also MPEP §2173.05(b) supporting this legal concept. The term "about" has almost always been found to be definite in Court challenges where it is a modifier for a numerical value, as is the case here. The instances where indefiniteness has been found have been where the term "about" is used as a modifier for other aspects that are also indefinite.

Applicants have further cited numerous examples from patents in this same specific art area supporting that one of ordinary skill in this art would reasonably understand the meaning the term "about" when used to modify a numerical pharmacokinetic parameter value (see, e.g., pages 4-10, of applicants' Response filed December 16, 2010). Applicants have also explained how the instant specification provides guidelines for assessing the meaning of the term "about" in the claims (see, e.g., pages 1-4, of applicants' Response filed December 16, 2010).

The Office has not presented any countervailing evidence to in any way contradict or rebut the substantial weight of evidence presented by Applicants.

In view of these arguments and evidence, in the Advisory Action mailed January 5, 2011, the Examiner appeared to acquiesce in Applicants' argument that the term "about" – by itself – in the instant claims is not indefinite. However, it was alleged that the usage of the term "about" in the phrases: "no more than about", "greater than about", "at least about" and "not greater than about", renders these phrases indefinite. Applicants submit that this does not logically follow. If the term "about" is definite in relation to a value, then phrases defining a range that is either higher or lower than the "about" value must also be definite. That is, when a clearly definite value is in question, e.g., the number 20, the recitation of "no more than about 20" cannot be indefinite if "about 20" is definite. Thus, if the value modified by "about" is definite, the additional recitations above which appear in the claims do not make the definite term indefinite.

The Advisory Action additionally states that the claims are indefinite because one could not determine where the claimed ranges begin and end. Again, applicants urge that this allegation arises from the improper requirement that the ranges give a precise mathematical value for the beginning and end. The MPEP and numerous decisions by the Board of Appeals and Court of Appeals for the Federal Circuit cited by Applicants make clear that this is a legally

deficient argument.

Regarding the term "substantially" in claim 15, applicants urge that the above arguments apply analogously. MPEP §2173.05(b)(D) specifically addresses this term citing cases which find the term does not give rise to indefiniteness. See also *Deering Precision Instruments, L.L.C. v. Vector Distribution Systems, Inc.*, 347 F.3d 1314, 68 USPQ2d 1716 (Fed. Cir. 2003), *cert. denied*, 540 U.S. 1184 (2004), *Ecolab Inc. v. Envirochem, Inc.*, 264 F.3d 1358, 1367, 60 USPQ2d 1173, 1179 (Fed. Cir. 2001) and *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 65 USPQ2d 1051 (Fed. Cir. 2002), stating: "Expressions such as 'substantially' are used in patent documents when warranted by the nature of the invention, in order to accommodate the minor variations that may be appropriate to secure the invention. Such usage may well satisfy the charge to 'particularly point out and distinctly claim' the invention, 35 U.S.C. § 112, and indeed may be necessary in order to provide the inventor with the benefit of his invention." The instant specification provides the necessary guidance for one of ordinary skill in the art to reasonably interpret the metes and bounds of the term "substantially" in relation to the fluctuation ratio recited in claim 15; see, e.g., page 8, para. 0042, and Example 7, pages 22-25, particularly Table 8 providing fluctuation ratio data and error parameters therefore.

For the above reasons, Applicants urge that the 35 U.S.C. §112 rejections made in the final Office Action are in clear error.

The 35 U.S.C. §103 Rejections

Applicants submit that the three grounds of rejection of the claims under 35 U.S.C. §103 based on combinations of Holman (U.S. Patent No. 6,277,875), Pospisilik (US 2002/0103240 and US 2004/0068119) and Vandercruys (WO 00/59477) are also clearly in error. The error is the same for each of the three rejections and all are discussed together.

The rejections are each clearly in error because they are made without due consideration of the full record. Specifically, the rejections are made without due consideration of the 37 C.F.R. §1.132 Declaration of Dr. Heimlich with accompanying documents and the MIRAPEX® information submitted by Applicants with the Response filed May 12, 2010. The declaration and other evidence provide a clear showing that Holman discloses immediate release formulations, not sustained release formulations. The declaration and accompanying evidence also provide a clear showing that one of ordinary skill in the art could not have had a reasonable expectation that the features of the several cited references could be combined in the manner suggested in the rejections to arrive at a sustained release pramipexole composition having the

features and properties recited in the instant claims. The final Office Action (page 7) alludes only once to the Heimlich Declaration but does not specifically address or refute any of the points made therein. The Advisory Action does not address the Heimlich Declaration evidence at all. The only substantive evidence on the record regarding reasonable expectation of success is the Heimlich Declaration evidence and it clearly and convincingly establishes that there was no reasonable expectation of success in combining the references in the manner suggested in the final Office Action to support obviousness. The failure to consider, refute or even raise doubt as to the Heimlich Declaration evidence supports that the 35 U.S.C. §103 rejections are clearly erroneous.

The specific reasons why the 35 U.S.C. §103 rejections are erroneous in view of the Heimlich Declaration evidence are believed to be clear from applicants' arguments in their Responses filed May 12, 2010 (see pages 11-17) and December 16, 2010 (pages 13-18). Applicants understand that arguments about the weighting of different showings are not an appropriate issue for a Pre-Appeal Brief Request. However, applicants believe that is not the issue here. The error here is that the clear showing made by applicants was not given any due consideration. The rejections should be withdrawn for this reason alone. However, although nothing further is necessary, the following summary of the main points of applicants' arguments and evidence is provided for the panel's further consideration.

Contrary to the allegations in the Office Actions and Advisory Action, the Holman compositions are immediate release formulations. The assertions in the Action that the Holman formulations are other than immediate release have no supporting evidence. No argument or evidence is provided to refute the objective reasoning provided in the Heimlich Declaration (paras. 5-9) showing how Holman's compositions are for immediate release. No argument at all is provided to refute applicants' further point (see pages 12-13 of the Response filed May 12, 2010) that Holman refers to "currently available" MIRAPEX® tablets (see col. 8, lines 49-57 and col. 11, lines 35-41) which at the time were unquestionably immediate release formulations (see the cited PDR excerpts referring to rapid absorption and achieving peak concentrations in two hours).

As confirmed in the Heimlich Declaration (paras. 10-12), the Pospisilik references merely refer to the possibility of providing controlled release pramipexole compositions. They provide no teachings which would give any suggestion to the specific formulations as claimed to provide such compositions or to achieve the specific dissolution, absorption and bioavailability parameters recited in the instant claims.

As discussed in the Heimlich Declaration (paras. 13-20), the Vandercruys reference fails to provide any reasonable expectation that a sustained release pramipexole composition could be provided with the specific formulations as claimed or the specific dissolution, absorption and bioavailability parameters as claimed. As explained by Dr. Heimlich, one of ordinary skill in the art would consider the Vandercruys teaching to be applicable to poorly soluble active agents distinct from pramipexole. One of ordinary skill in the art would understand that teachings applicable to providing sustained release of poorly soluble active agents could not be reasonably expected to succeed with a highly soluble drug such as pramipexole, since solubility would be expected to greatly impact release, absorption and bioavailability characteristics.

The Office has not presented any countervailing evidence to in any way contradict or rebut the substantial weight of evidence presented by Applicants, including that presented by Applicants' formulation expert Dr. Heimlich.

Applicants urge that the 35 U.S.C. §103 rejections made in the final Office Action are in clear error because they are made without due consideration of the full record.

It is submitted that the application is in condition for allowance. But the Examiner is kindly invited to contact the undersigned attorney to discuss any unresolved matters.

Respectfully submitted,

Dated: January 24, 2011

/Seth H. Jacobs/
Seth H. Jacobs
Reg. No. 32,140
Phone: (212) 733-3678